

## REMARKS

Applicants have carefully considered this Application in connection with the Examiner's Office Action, and respectfully request reconsideration of this Application in view of the above amendments and the following remarks.

Claims 1-41, and 58-73 are withdrawn.

Claims 42 and 46 are currently amended.

Claims 43-45, 47-50, and 54-55, have been cancelled.

Claims 42 and 46 have been amended to recite, "a dried blood or plasma sample," which is supported in paragraph [0090].

Claim 42 has been amended to correct an antecedent basis issue in "the human subject."

Claim 42 has also been amended to remove the term "animal" and instead recite, "human subject."

New Claim 74 has been added.

### **I. Claim Rejections under 35 USC §112**

A. The Examiner has rejected Claims 42, 46, 51-53, 56, and 57 under 35 USC §112, second paragraph, for being indefinite due to the term, "a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test."

Applicants respectfully submit that this is, in fact, supported by the specification and does not constitute new matter. In Example 3, which describes a multiplex test conducted using  $\alpha$ -iduronidase,  $\alpha$ -glucosidase, LAMP-1 and sapsoin C, paragraph [0097] describes the improved

accuracy obtained by calculating ratios of a-glucosidase to LAMP-1, and a-iduronidase to LAMP-1. Paragraph [0095] shows that MWU Test values were used to determine significance in deviations from control values.

Therefore, the claim clearly describes the limitations of the method which are laid out in the specification as originally filed. Applicants believe that this will overcome the Examiner's objection.

**B.** The Examiner has rejected Claims 42, 46, 51-53, 56, and 57 under 35 USC §112, second paragraph, for being indefinite because the claims recite all biological samples or any and all target animals.

Applicants have amended Claim 42 to recite a human subject. Claim 46 has been amended to recite a sample which is dried blood or plasma. Therefore, the claims no longer recite all biological samples or any and all target animals, and Applicants believe the rejection is overcome.

**C.** The Examiner has stated in the Advisory Action of November 30, 2010, that it is unclear how the first and second fluorophores are related to detection. Applicants respectfully submit that this is shown in Figure 10, and described in paragraphs [0074] and [0089] of the specification. In the currently disclosed assay, each microsphere is labeled internally with a fixed ratio of two different fluorophores (110 in Figure 10), which combine to generate a detectable fluorescent signal. This allows for creation of microspheres having a multitude of detection signals by creating microspheres with varying ratios of the two fluorophores. This is useful in multiplex assays because many microspheres with non-overlapping signals can be used, each to detect a different antigen.

Each microsphere is conjugated to a target LSD capture antibody (120 in Figure 10). When the target LSD antigen (130 in Figure 10) is present, the target LSD capture antibody (120 in Figure 10) binds it, and the detection LSD antibody (140 in Figure 10) also binds it. The detection LSD antibody (140 in Figure 10) is conjugated to a detection molecule (150 in Figure 10). In this situation (i.e. when the LSD antigen is present), two signals are detectable from the microsphere as it passes through a flow cytometer: 1) the signal from the fluorophores in the microsphere; and 2) the

signal from the detection molecule. This allows indirect detection of the LSD antigen, because it is known to be present when the microsphere signal and the detection molecule are both present as the microspheres are processed in a flow cytometer. It is noted that while a flow cytometer presents one option for detecting such an assay, it would also be possible to detect the sandwich assay in other formats, including microtitre plates.

## II. Conclusion

Applicants respectfully submit that, in light of the foregoing comments, all pending claims are in condition for allowance. A Notice of Allowance is therefore requested.

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,



---

T. Ling Chwang  
Reg. No. 33,590  
Jackson Walker L.L.P.  
901 Main Street, Suite 6000  
Dallas, Texas 75202  
Tel: (214) 953-5959  
Fax: (214) 661-6870



---

Date